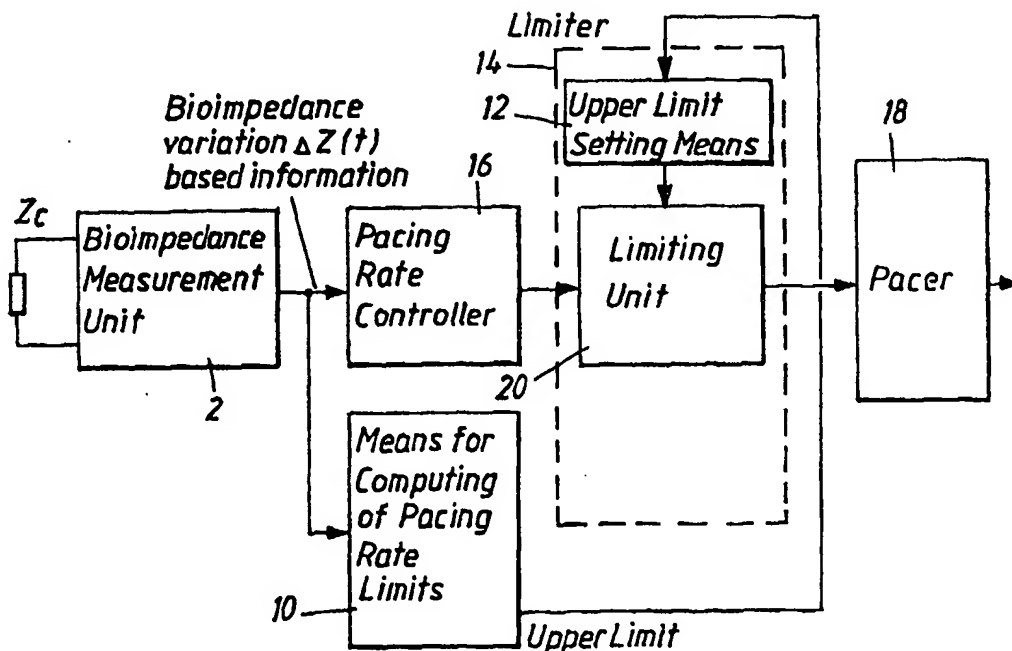




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(54) Title: A RATE ADAPTIVE PACEMAKER



(57) Abstract

A rate adaptive pacemaker comprises means (2) for determining the demand of a patient's organism, a pacing rate controlling means (16) for controlling the pacing rate in response to the patient's demand, and a pacing rate limiting means (20) for preventing the pacing rate from becoming too high. The pacing rate limiting means is adapted to limit the pacing rate upwards such that a predetermined relation is maintained between energy supplied to the myocardium and energy consumed by the myocardium.

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A RATE ADAPTIVE PACEMAKER.

Technical field

The present invention relates to a rate adaptive pacemaker comprising a means for determining the demand of the patient's organism, a pacing rate controlling means for
5 controlling the pacing rate in response to the patient's demands and a pacing rate limiting means for preventing the pacing rate from becoming too high.

Background Art

10 Too high pacing rates can appear in a rate adaptive pacemaker due to the physical demand of the patient's organism and heart. This may cause lack of oxygen supply to the myocardium. Thus, in certain conditions the heart may not be able to satisfy the physiological needs of the patient's
15 organism and heart if the pacing rate is not limited.

Several different proposals for limiting the pacing rate upwards have been presented. Thus in e.g. US-A-5,350,409 a rate adaptive pacemaker is described having an upper pacing
20 limit programmed beyond which rate the pacemaker will not generate and deliver stimulation pulses. US-A-5,792,195 discloses an acceleration sensed safe upper rate envelope for calculating the haemodynamic upper rate limit for a rate adaptive pacemaker. From the output signal from an accelero-
25 meter the time of occurrence of a specific heart sound in relation to a previously occurring ventricular depolarization event is then derived and this heart sound information is used to establish a haemodynamic upper rate limit for the pacemaker. Also EP-0 879 618 A1 describes a rate modulated
30 heart stimulator having a programmable maximum sensor rate. This heart stimulator also includes an ischemia detector and in response to the detection of an ischemia the maximum allowable stimulation rate is decreased.

35 The limit values are determined from patients' diagnosis and the setting can be either constant or externally programmable.

The purpose of the present invention is to propose a new way of continuously automatically limiting the pacing rate upwards according to the current ability of the patient's heart.

Disclosure of the Invention

This purpose is obtained by a rate adaptive pacemaker according to claim 1.

Thus, in the pacemaker according to the invention the myocardium energy consumption and energy supply can be kept in balance, and since this relation, and not the heart rate, is of primary importance, the patient can feel more healthy and comfortable in various everyday life conditions, also in conditions of active work.

Preferred embodiments are set forth in the dependent claims.

According to an advantageous embodiment of the pacemaker according to the invention the pacing rate limiting means is adapted to limit the pacing rate upwards such that the energy consumed by the myocardium always is less than the energy supplied to the myocardium. In this way lack of oxygen supply to the myocardium is avoided.

According to another advantageous embodiment of the pacemaker according to the invention said pacing rate limiting means includes an upper limit setting means for setting an upper limit value for the pacing rate, and an upper limit determining means to determine the relation between energy supplied to the myocardium and energy consumed by the myocardium for calculating an upper pacing rate limit value from said relation for supply to said upper limit setting means. Thus, in this way the actual pacing rate is continuously compared to a set upper limit value and the actual pacing rate is limited to a maximum value equal to this limit value.

According to still other advantageous embodiments of the pacemaker according to the invention said pacing rate limiting means is adapted to limit the pacing rate such that the inequality

$$(t_{\text{diast,rest}}/t_{\text{diast}}) \cdot (SV/SV_{\text{rest}}) < CR$$

(1)

is satisfied, alternatively said upper limit determining means is adapted to determine actual coronary resistance ratio (CRR) from the equation

$$\text{supplied energy} = \text{consumed energy} \quad (2)$$

and determine an upper pacing rate limit from the relation between actual coronary resistance ratio (CRR) and coronary reserve (CR), or said upper limit determining means is adapted to determine the upper pacing rate limit value from the equation

$$\begin{aligned} \text{upper pacing rate limit} = \\ (60 \cdot CR) / [t_{\text{diast,rest}} \cdot (SV/SV_{\text{rest}}) + CR \cdot t_{\text{syst}}] \end{aligned} \quad (3)$$

where $t_{\text{diastrest}}$ denotes diastolic duration for the patient in rest conditions, t_{diast} actual diastolic duration for the patient, SV and SV_{rest} actual stroke volume and stroke volume for the patient in rest conditions respectively, and t_{syst} the actual systolic duration. The term "rest condition" is intended to cover not only resting by lying down but also other standard defined low load conditions such as sitting. A bioimpedance measurement unit is preferably provided to measure the intracardiac bioimpedance as a function of time and determine therefrom actual stroke volume SV and actual diastolic and systolic duration t_{diast} and t_{syst} respectively. Since the electrical bioimpedance can be effectively used to determine cardiac parameters, in particular the parameters mentioned above can be obtained from the time variation of the bioimpedance measured between the tip of an intracardiac electrode and the housing of a pacemaker when an excitation

current proceeds from the electrode tip, the parameters needed for preventing the pacing rate from becoming too high can be obtained in a very convenient manner by using a standard pacing lead.

5

Brief Description of the Drawings

The invention will now be described more in detail with reference to the enclosed drawings on which

10

fig. 1a shows the ventricular pressure-volume loop for a heart rate of 60 beats per minute,

fig. 1b shows the variation of arterial pressure as a function of time for the same heart rate,

15

fig. 2a and b show the corresponding pressure-volume loop and time variation curve for a twice as high heart rate of 120 beats per minute,

fig. 3 is a block diagram of an embodiment of the pacemaker according to the invention, and

20

fig. 4 illustrates the principle of bioimpedance measurement between the tip of an intracardiac electrode and the metal housing of the pacemaker.

Fig. 5 illustrates the relationships of the cardiac parameters of interest.

Description of Preferred Embodiments

25

As mentioned above, according to one embodiment of the pacemaker according to the invention an upper limit value for the pacing rate is determined based on a balance between the energy consumption of the myocardium and the energy supplied to the myocardium for high patient workloads.

30

Since the oxygen demand, or demanded energy consumption which is equal to the work of myocardium, is well correlated to the area S_{dem} within the ventricular pressure-volume loop shown in figure 1a, the following equations are valid

35

$$W = S_{\text{dem}} = \bar{\Delta} \bar{P} \times SV \quad (4)$$

where W denotes the work of myocardium, $\bar{\Delta P}$ the mean value of the ventricular pressure variations during a cardiac cycle, and SV the stroke volume.

5 Further, in figures 1 and 2, P_{as} denotes the atrial systolic pressure, P_{ves} the ventricular systolic pressure, P_{ved} the ventricular diastolic pressure and P_{ad} the atrial diastolic pressure.

10 The energy supplied to the myocardium can be derived from the time response curve of the arterial pressure shown in figure 1b. The area S_{supp} is namely proportional to the supplied energy E . Thus

$$E = S_{supp} \times K = (\bar{\Delta P} \times t_{diast}) \times K \quad (5)$$

15 where t_{diast} denotes the diastolic duration of the patient's heart and K a coefficient essentially representing the conductance for energy influx into the myocardium. The coefficient K can be expressed as

$$K = \frac{C_{O_2} \cdot k_{O_2}}{R} \quad (6)$$

20 where C_{O_2} denotes the difference of the blood oxygen concentration in the artery and vein, i.e. the oxygen uptake, k_{O_2} the energy productivity of blood oxygen, and R the hydraulic resistance of the coronary arteries.

25 The energy balance $W = E$ results in

$$\frac{SV}{t_{diast}} = K \quad (7)$$

Thus, if

$$\frac{SV}{t_{diast}} > K \quad (8)$$

the pacing rate must be reduced, because the myocardium does not get sufficient energy, though the patient's organism, i.e. body, can demand even an increase of the pacing rate.

5 From figures 1 and 2 it appears that the area S_{dem} , representing energy consumed by the myocardium, increases when the heart rate increases, whereas the area S_{SUPP} which is proportional to the energy supplied to the myocardium decreases with increasing heart rate. Thus it is obvious that
10 for a certain heart rate energy balance can no longer be maintained.

The energy supplied to the myocardium can also be expressed as

$$15 \quad E = V_{\text{mc}} \cdot \text{AVD} \cdot k_{\text{O}_2} \quad (9)$$

where V_{mc} denotes the blood volume flowing through the myocardium during one cardiac cycle and AVD the arteriovenous blood oxygen difference, i.e. equal to the blood oxygen uptake CO_2 .

20

The blood volume flowing V_{mc} can be expressed as

$$V_{\text{mc}} = \int_0^{t_{\text{diast}}} f_c(t) \cdot dt = \bar{f}_c \cdot t_{\text{diast}} \quad (10)$$

where $f_c(t)$ denotes the blood flow per time unit through the myocardium and \bar{f}_c the mean value of this blood flow.

25

From equations (9) and (10) the following expression is obtained for the supplied energy E .

$$E = \bar{f}_c \cdot \text{AVD} \cdot k_{\text{O}_2} \cdot t_{\text{diast}} \quad (11)$$

since

$$30 \quad f_c = \frac{\bar{P}}{R} \quad (12)$$

the supplied energy E can be expressed as

$$E = \frac{\bar{P}}{R} \cdot (AVD \cdot k_{O_2} \cdot t_{diast}) \quad (13)$$

and consequently the coronary resistance as

$$R = \frac{AVD \cdot k_{O_2} \cdot t_{diast}}{SV} \quad (14)$$

in the case of energy balance, i.e. $E = W$.

5

A well known parameter expressing the work ability of the heart is the coronary reserve CR, which can be expressed as

$$CR = \frac{R_{rest}}{R_{min}} \quad (15)$$

10

where R_{rest} denotes the resistance of the coronary arteries for the patient in rest conditions and R_{min} the minimum value of this resistance. Thus the coronary reserve CR expresses directly the ability of coronary arteries to widen during work, the resistance R then being reduced from R_{rest} to its minimum value R_{min} . The coronary reserve varies in a healthy heart from about 4 to 6,, but in the case of coronary artero-

15

sclerosis it is lower, typically less than 2.

The current actual value of the ratio R_{rest}/R is called coronary resistance ratio CRR and equals

20

$$CRR = \frac{t_{diast,rest} \cdot AVD_{rest} \cdot k_{O_2} \cdot SV}{t_{diast} \cdot AVD \cdot k_{O_{2,rest}} \cdot SV_{rest}} \quad (16)$$

Since $k_{O_2, rest} = k_{O_2}$ and by denoting

$$\frac{AVD_{rest}}{AVD} = q \quad (17)$$

q can vary from 1.0 to 0.5, q is decreasing significantly below 1 only in case of anaerobic work of the myocardium.

Arteriovenous difference AVD of the oxygen concentration in blood, i.e. oxygen uptake, does not vary significantly with physical load up to the load allowable for the pacemaker patients, i.e. up to anaerobic load limit. This is so due to
 5 autonomous regulation of blood circulation inside the myocard.

Thus, the coronary resistance ratio CRR can be expressed as

$$\text{CRR} = \frac{t_{\text{diast,rest}}}{t_{\text{diast}}} \cdot \frac{\text{SV}}{\text{SV}_{\text{rest}}} \cdot q \quad (18)$$

The coronary resistance ratio CRR expresses the degree of
 10 utilisation of the coronary reserve CR and when $\text{CRR} = \text{CR}$ the complete coronary reserve is utilized, which means that the ability of the heart to maintain the energy balance $E = W$ has reached near to its safe limit. If the coronary resistance ratio CRR becomes larger than the coronary reserve CR the
 15 pacing rate must be limited.

For $q = 1$ there is no risk for overpacing and for safe limitation of the pacing rate it is suitable to avoid anaerobic operation of the myocardium. Thus the following
 20 inequality can be used as criteria for pacing rate limitation.

$$\frac{t_{\text{diast,rest}}}{t_{\text{diast}}} \cdot \frac{\text{SV}}{\text{SV}_{\text{rest}}} < \text{CR} \quad (19)$$

From the equation

$$\frac{t_{\text{diast,rest}}}{t_{\text{diast}}} \cdot \frac{\text{SV}}{\text{SV}_{\text{rest}}} = \text{CR} \quad (20)$$

25 and the relation

$$T = t_{\text{diast}} + t_{\text{syst}} \quad (21)$$

where T denotes the duration of the cardiac cycle in seconds, the following expression is obtained for the upper pacing rate limit in beats per minute

$$\text{upper pacing rate limit} = 60/T = (60 \cdot CR) / [t_{\text{diast, rest}} \cdot (SV/SV_{\text{rest}}) + CR \cdot t_{\text{syst}}] \quad (22)$$

The parameters stroke volume SV, and the diastolic or systolic durations t_{diast} or t_{syst} are preferably determined from measured time variations of the electric intracardiac bioimpedance, cf. below, and the coronary reserve is obtained by standard physical stress test as using veloergometers or treadmills.

Figure 3 is a block diagram of an embodiment of the pacemaker according to the invention comprising a bioimpedance measurement unit 2 for measuring the time variation of the electric intracardiac bioimpedance $Z_c(t)$. This type of measurements is well known, see e.g. "Design of Cardiac Pacemakers", edited by John G. Webster, IEEE Press, 1995, pp. 380-386 and US-A-5,154,171, 5,280,429, 5,282,840 and 5,807,272. Thus the time variation of the intracardiac bioimpedance can be measured between the tip 4 of the intracardiac electrode 6 and the housing 8 of the pacemaker, when an excitation current is fed from the electrode tip 4, as schematically illustrated in figure 4. Thus a standard pacing lead can be used for this measurement.

From the measured time variations $\Delta Z_c(t)$ the parameters for calculating the upper pacing rate limit according to equation (22) above, or for checking the inequality (19), is determined in computing means 10, see figure 3.

The calculated upper limit value is supplied to an upper limit setting means 12 of a pacing rate limiter 14.

A pacing rate controller 16 is also provided for controlling the pacing rate of the pacer or pulse generator 18 in

response to the patient's demands. In a limiting unit 20 of the limiter 14 the demanded pacing rate is compared to the set upper limit pacing rate and the actual pacing rate is limited to the set upper limit value if the demanded pacing rate reaches this limit value. Thus in the pacemaker according to the invention an upper limit value for the pacing rate is continuously automatically determined and it is continuously automatically verified that the actual pacing rate does not exceed the present upper limit value. Alternatively, the pacemaker can be modified to continuously monitor that the inequality (19) above is satisfied.

Above bioimpedance measurements are described for determining necessary parameters like stroke volume SV, diastolic or systolic durations t_{diast} or t_{syst} . These parameters can, however, also be determined by other techniques. Thus these parameters can be determined from measured ECG's, by ultrasound technique, etc.

The relationships of the cardiac parameters of interest are illustrated in Fig. 5:

If load increases from Rest to some level (e.g. 100W), the stroke volume SV increases 1.2 to 1.5 times, and the diastole time $t_{\text{diast}} = t_{\text{cycle}} - t_{\text{syst}}$ decreases rapidly with the HR (e.g. 3x).

Falling of the coronary arterial hydraulic resistance due to widening of the blood vessels with the increase of myocardial work $W = S_{\text{dem}}$ compensates the decrease of the myocardial energy supply

$$E = S_{\text{suppl}} \cdot K (C_{O_2}; k_{O_2}; R).$$

The compenstion ability can be expressed by the coronary reserve $CR = 2 \dots 5$ for a typical patient.

Claims

1. A rate adaptive pacemaker comprising a means (2) for
5 determining the demand of a patient's organism, a pacing rate
controlling means (16) for controlling the pacing rate in
response to the patient's demand, and a pacing rate limiting
means (20) for preventing the pacing rate from becoming too
10 high, **characterized in** that said pacing rate limiting means
(14) is adapted to limit the pacing rate upwards such that a
predetermined relation is maintained between energy supplied
to the myocardium and energy consumed by the myocardium.

2. The pacemaker according to claim 1, **characterized in**
15 that said pacing rate limiting means is adapted to limit the
pacing rate upwards such that the energy consumed by the
myocardium always is less than energy supplied to the
myocardium.

3. The pacemaker according to claims 1 or 2, **characterized**
20 **in** that said pacing rate limiting means is adapted to limit
the pacing rate such that the inequality

$$(t_{\text{diast, rest}}/t_{\text{diast}}) \cdot (SV/SV_{\text{rest}}) < CR$$

is satisfied, where $t_{\text{diastrest}}$ denotes diastolic duration for
the patient in rest conditions, t_{diast} actual diastolic
25 duration for the patient, SV and SV_{rest} actual stroke volume
and stroke volume for the patient in rest conditions
respectively, and CR the coronary reserve.

4. The pacemaker according to any of the preceding claims,
characterized in that said pacing rate limiting means
30 includes an upper limit setting means for setting an upper
limit value for the pacing rate, and an upper limit
determining means for determining the relation between energy
supplied to the myocardium and energy consumed by the
myocardium for calculating an upper pacing rate limit value
35 from said relation for supply to said upper limit setting
means.

5. The pacemaker according to claim 4, **characterized in** that said upper limit determining means includes an energy determining means for determining the energy supplied to the myocardium and the energy consumed by the myocardium respectively, and a comparison means for comparing supplied energy and consumed energy for determining said relation.

6. The pacemaker according to claim 5, **characterized in** that said energy determining means is adapted to determine consumed energy as the product of mean value of ventricular pressure variations during a cardiac cycle and stroke volume.

7. The pacemaker according to claims 5 or 6, **characterized in** that said energy determining means is adapted to determine supplied energy from the time response curve of the arterial pressure during diastole.

8. The pacemaker according to claim 4, **characterized in** that said upper limit determining means is adapted to determine actual coronary resistance ratio (CRR) from the equation

$$\text{supplied energy} = \text{consumed energy}$$

and determine an upper pacing rate limit value from the relation between actual coronary resistance ratio (CRR) and coronary reserve (CR).

9. The pacemaker according to any of the claims 4 - 8, **characterized in** that said upper limit determining means is adapted to determine the upper pacing rate limit value from the equation

$$\text{upper pacing rate limit} = (60 - CR) / [t_{\text{diast, rest}} \cdot (SV / SV_{\text{rest}}) + CR \cdot t_{\text{syst}}]$$

where CR

denotes the coronary reserve, $t_{\text{diastrest}}$ diastolic duration for the patient in rest conditions, SV and SV_{rest} actual stroke volume and stroke volume for the patient in rest conditions respectively, and t_{syst} the actual systolic duration.

10. The pacemaker according to any of the claims 3 - 9, **characterized in** that a bioimpedance measurement unit is provided to measure the intracardiac bioimpedance as a function of time and determine therefrom actual stroke volume

SV and actual diastolic or systolic durations t_{diast} or t_{syst} respectively.

11. The pacemaker according to any of the claims 3 - 9, characterized in that an ECG measuring and analyzing unit is provided to measure ECG and determine therefrom actual stroke volume SV and actual diastolic or systolic durations t_{diast} or t_{syst} respectively.

Fig. 1a

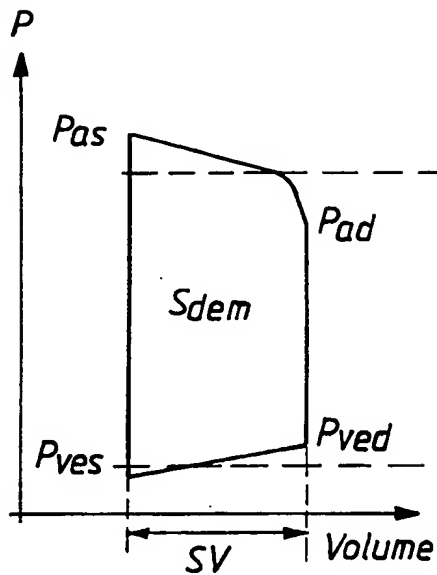


Fig. 1b

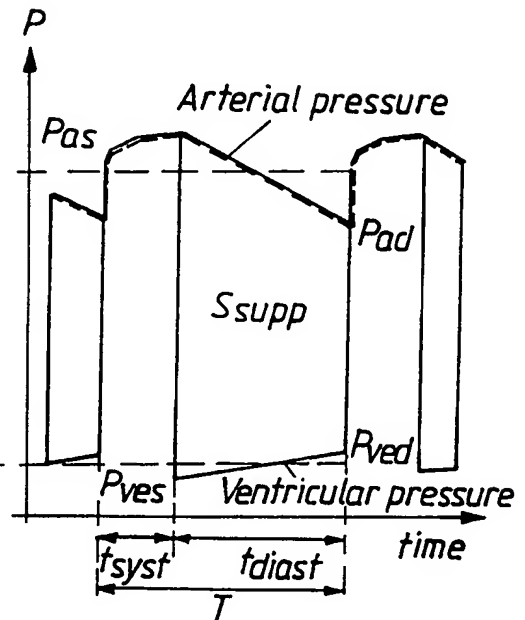


Fig. 2a

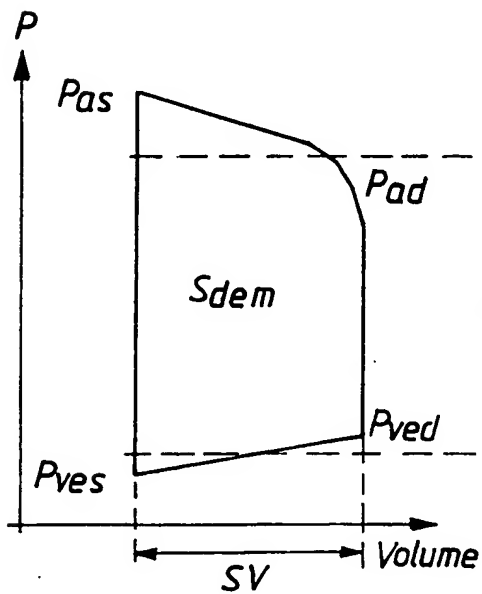
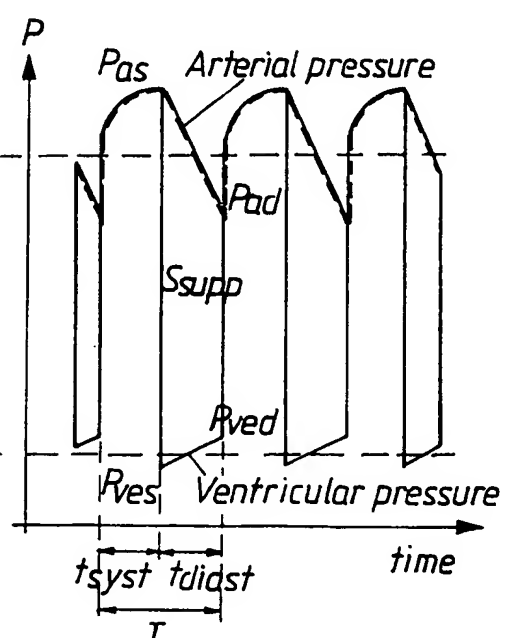
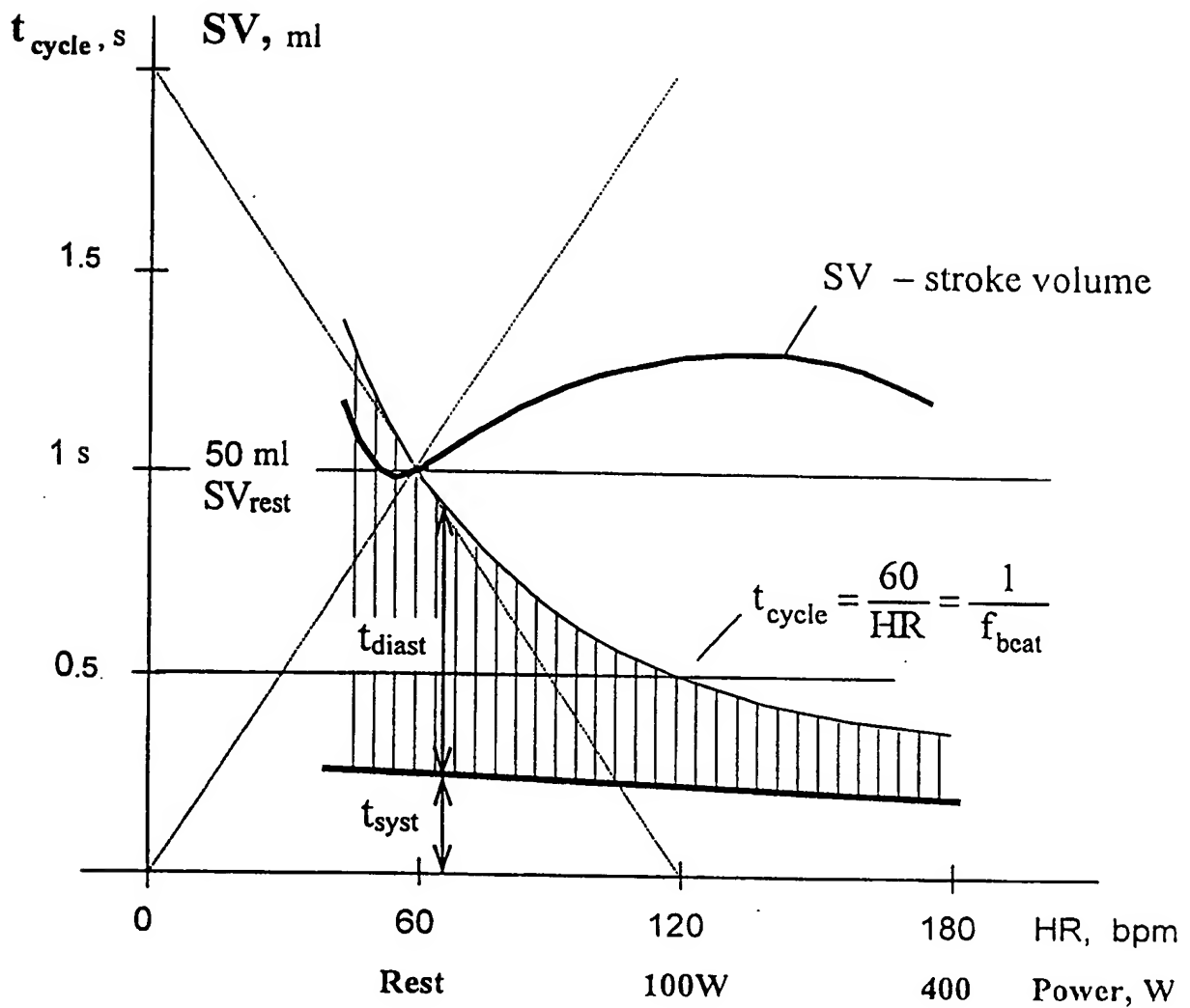


Fig. 2b



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Fig. 5



INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 00/00573

A. CLASSIFICATION OF SUBJECT MATTER

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B. FIELDS SEARCHED

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Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

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Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5305745 A (FRED ZACOUTO), 26 April 1994 (26.04.94), column 40, line 24 - column 41, line 63 --	1,2,4,5,10
D,A	EP 0879618 A1 (PACESETTER AB), 25 November 1998 (25.11.98), abstract -- -----	1-10



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INTERNATIONAL SEARCH REPORT
Information on patent family members

02/12/99

International application No.

PCT/SE 00/00573

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5305745 A	26/04/94	AT 103498 T CA 1327838 A DE 68914199 D,T EP 0348271 A,B FR 2632533 A,B FR 2637807 A,B JP 2786271 B JP 3055032 A	15/04/94 15/03/94 14/07/94 27/12/89 15/12/89 20/04/90 13/08/98 08/03/91
EP 0879618 A1	25/11/98	AU 710718 B AU 3469997 A EP 0907384 A JP 10263093 A NO 986048 A NZ 333225 A PL 330714 A SE 9701121 D SE 9804441 A	30/09/99 14/01/98 14/04/99 06/10/98 26/02/99 28/05/99 24/05/99 00/00/00 18/02/99

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